Curriculum vitae

Name: Yasumichi Hitoshi, MD. Ph.D.

Born: November 21, 1961. Kumamoto, Japan

Citizenship: Japan

Present Position: Director, Oncology

Present address: Rigel pharmaceutical Inc.,
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South San Francisco
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Professional experience:

2003.7-present Director, Oncology

Department of Cell Biology

Rigel pharmaceutical Inc.

Research and Development: Identification and validation of drug targets for cancer therapy, and development of anti-cancer drugs.

2002.7-2003.7 Associate director, Project leader

Department of Cell Biology,

Rigel pharmaceutical Inc.

Research: Validation of drug targets for inhibition of tumor cell growth or sensitization of tumor cells to the effects of chemotherapeutic agents via cell cycle regulation.

2002.1-2002.7 Group leader, Project leader

Department of Cell Biology,

Rigel pharmaceutical Inc.

Research: Validation of drug targets for inhibition of tumor cell growth or sensitization of

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tumor cells to the effects of chemotherapeutic agents via cell cycle regulation.

1998.12-2001.12 Senior scientist, Project leader
Department of Cell Biology,
Rigel pharmaceutical Inc.
Research: Identification of proteins and peptides that play an important role in cell cycle regulation of specific tumor cells using retroviral functional screens.

1998.2-1998.12 Senior scientist
Department of Cell Biology,
Rigel pharmaceutical Inc.
Research: Characterization of a membrane receptor, Toso, which inhibit TNF receptor family-induced apoptosis.

1995.3-1998.2 Postdoctoral Fellow
Department of Molecular Pharmacology, Stanford University.
Research: Analysis of signaling pathway using high titer retrovirus.
Scientific Advisor: Assistant Professor Garry P. Nolan

1992.1-1995.3 Postgraduate Research Associate
Department of Immunology,
The Institute of Medical Science,
The University of Tokyo.
Scientific Advisor: Professor Kiyoshi Takatsu
Research: Cellular mechanism of development of a retrovirus-induced immunodeficiency syndrome (MAIDS)

1991.4-1991.12 Postgraduate Research Associate
Department of Biology,
The Institute for Medical Immunology,
Kumamoto University Medical School.
Scientific Advisor: Professor Kiyoshi Takatsu
Research: Signal transduction through IL-5 receptor and involvement of Xid defect in the receptor system.

Education:

Medical School

1981-1987 Kumamoto University Medical School

Graduate School

1987-1991 Department of Biology,
The Institute for Medical Science,
Kumamoto University Medical School
Research: Immunology
Scientific Advisor: Professor Kiyoshi Takatsu
Thesis Dissertation: Role of interleukin 5 and its receptor in the immune system.

Membership of learned societies:

American Association for Cancer Research
The American society for Cell Biology

Honors and Fellowships

Special Fellow of The Japanese Ministry of Education, Culture and Science,
April 1990-March 1991.
The Uehara Memorial Foundation Fellowship, April 1995-March 1996.

Publications

1. Mita, S., Harada, N., Naomi, S., **Hitoshi, Y.**, Sakamoto, K., Akagi, M., Tominaga, A. & Takatsu, K., (**1988**). Receptors for T cell-replacing factor / Interleukin 5 Specificity, quantitation, and its implication. J. Exp. Med., 168, 863 - 878.

2. Jankovic, D.L., Abehsira-Amar, O., Korner, M., Roth, C., **Hitoshi, Y.**, Takatsu, K. & Theze, J., (**1988**). IL-4, but not IL-5, can act synergistically with B cell activating factor (BCAF) to induce proliferation of resting B cells. Cell. Immunol., 117, 165 - 176.

3. **Hitoshi, Y.**, Mita, S., Tominaga, A., Kikuchi, Y., Sonoda, E., Takatsu, K. & Watanabe, Y., (**1989**). Interferon-gamma inhibits the proliferation but not the differentiation of murine B cells in response to IL-5. Int. Immunol., 1, 185 - 190.

4. Tominaga, A., Mita, S., Kikuchi, Y., **Hitoshi, Y.**, Takatsu, K., Nishikawa, S.-I. & Ogawa, M., (**1989**). Establishment of IL-5-dependent early B cell lines by long-term bone marrow cultures. Growth Factors, 1, 135 - 146.

5. Matsumoto, R., Matsumoto, M., Mita, S., **Hitoshi, Y.**, Ando, M., Araki, S., Yamaguchi, N., Tominaga, A. & Takatsu, K., (**1989**). Interleukin-5 induces maturation but not class switching of surface IgA-positive B cells into IgA-secreting cells. Immunology, 66, 32 - 38.

6. Sonoda, E., Matsumoto, R., **Hitoshi, Y.**, Ishii, T., Sugimoto, M., Araki, S., Tominaga, A., Yamaguchi, N. & Takatsu, K., (**1989**). Transforming growth factor β induces IgA production and acts additively with interleukin 5 for IgA production. J. Exp. Med., 170, 1415 - 1420.

7. Mita, S., Tominaga, A., **Hitoshi, Y.**, Sakamoto, K., Honjo, T., Akagi, M., Kikuchi, Y., Yamaguchi, N. & Takatsu, K., (**1989**). Characterization of high-affinity receptors for interleukin 5 on interleukin 5-dependent cell lines. Proc. Natl. Acad. Sci. USA, 86, 2311 - 2315.

8. Enokihara, H., Furusawa, S., Nakakubo, H., Kajitani, H., Nagashima, S., Saito, K., Shishido, H., **Hitoshi, Y.**, Takatsu, K., Noma, T., Shimizu, A. & Honjo, T., (**1989**). T cells from eosinophilic patient produce interleukin-5 with interleukin-2 stimulation. Blood, 73, 1809 - 1813.

9. Takaki, S., Tominaga, A., **Hitoshi, Y.**, Mita, S., Sonoda, E., Yamaguchi, N. & Takatsu, K., (**1990**). Molecular cloning and expression of the murine interleukin-5 receptor. EMBO J., 9, 4367-4374.

10. Murata, Y., Yamaguchi, N., **Hitoshi, Y.**, Tominaga, A. & Takatsu, K., (**1990**). Interleukin 5 and interleukin 3 induce serine and tyrosine phosphorylation of several cellular proteins in an interleukin 5-dependent cell line. Biochem. Biophys. Res. Commun., 173, 1102-1108.

11. Mita, S., Kikuchi, Y., **Hitoshi, Y.**, Sakamoto, K., Tominaga, A. & Takatsu, K., (**1990**). Cyclosporin A preferentially inhibits the differentiation of murine B cells in response to IL-5 and its restoration by IL-6. Kumamoto Med. J., 42, 73-86.

12. **Hitoshi, Y.**, Yamaguchi, N., Mita, S., Sonoda, E., Takaki, S., Tominaga, A. & Takatsu, K., (**1990**). Distribution of IL-5 receptor-positive B cells : Expression of IL-5 receptor on Ly-1(CD5)$^+$ B cells. J. Immunol., 144, 4218 - 4225.

13. Enokihara, H., Kajitani, H., Nagashima, S., Tsunogake, S., Takano, N., Saitou, K., Furusawa, S., Shishido, H., **Hitoshi, Y.** & Takatsu, K., (**1990**). Interleukin 5 activity in sera from patients with eosinophilia. Brit. J. Haematol., 75, 458 - 462.

14. Yamaguchi, Y., Suda, T., Shiozaki, H., Miura, Y., **Hitoshi, Y.**, Tominaga, A., Takatsu, K. & Kasahara, T., (**1990**). Role of IL-5 in IL-2-induced eosinophilia In vivo and in vitro expression of IL-5 mRNA by IL-2. J. Immunol., 145, 873 - 877.

15. Yamaguchi, N., **Hitoshi, Y.**, Mita, S., Hosoya, Y., Murata, Y., Kikuchi, Y., Tominaga, A. & Takatsu, K., (**1990**). Characterization of the murine interleukin 5 receptor by using a monoclonal antibody. Int. Immunol., 2, 181 - 187.

16. Yamaguchi, Y., Suda, T., Suda, J., Eguchi, M., Miura, Y., Mita, S., **Hitoshi, Y.**, Tominaga, A. & Takatsu, K., (**1990**). Analysis of eosinophil-predominant colonies formed by human hemopoietic precursor cells in the presence of purified interleukin-5. Acta Haematol. Jpn, 53, 688 - 698.

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19. Yamaguchi, N., **Hitoshi, Y.**, Takaki, S., Murata, Y., Migita, M., Kamiya, T., Minowada, J., Tominaga, A. & Takatsu, K., (**1991**). Murine interleukin 5 receptor isolated by immunoaffinity chromatography: comparison of determined N-terminal sequence and deduced primary sequence from cDNA and implication of a role of the intracytoplasmic domain. Int. Immunol., 3, 889-898.

20. **Hitoshi, Y.**, Yamaguchi, N., Korenaga, M., Mita, S., Tominaga, A. & Takatsu, K., (**1991**). In vivo administration of antibody to murine IL-5 receptor inhibits eosinophilia of IL-5 transgenic mice. Int. Immunol., 3, 135-139.

21. Migita, M., Yamaguchi, N., Mita, S., Higuchi, S., **Hitoshi, Y.**, Yoshida, Y., Tomonaga, M., Matsuda, I., Tominaga, A. & Takatsu, K., (**1991**). Characterization of the human IL-5 receptors on eosinophils. Cell. Immunol., 133, 484-497.

22. Korenaga, M., **Hitoshi, Y.**, Yamaguchi, N., Sato, Y., Takatsu, K. & Tada, I., (**1991**). The role of interleukin-5 in protective immunity to Strongyloides venezuelensis infection in mice. Immunology, 72, 502-507.

23. Sonoda, E., **Hitoshi, Y.**, Yamaguchi, N., Ishii, T., Tominaga, A., Araki, S. & Takatsu, K., (**1992**). Differential Regulation of IgA Production by TGF-β and IL-5: TGF-β induces Surface IgA-Positive Cells Bearing IL-5 Receptor, Whereas IL-5 Promotes Their Survival and Maturation into IgA-Secreting Cells. Cell. Immunology, 140, 158-172.

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32. Korenaga, M., **Hitoshi, Y.**, Takatsu, K. & Tada, I., (**1994**). Regulatory effect of anti-interleukin 5 monoclonal antibody on intestinal worm burden in a primary infection with Strongyloides Venezuelensis in mice. Int. J. Parasitology, 24, 951-957.

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42. Gururaja T, Li W, Catalano S, Bogenberger J, Zheng J, Keller B, Vialard J, Janicot M, Li L, **Hitoshi Y**, Payan DG, Anderson DC. (**2003**) Cellular interacting proteins of functional screen-derived antiproliferative and cytotoxic peptides discovered using shotgun peptide sequencing. Chem Biol., 10, 927-937.

43. Lorens, J.B., Pearsall, D.M., Swift, S.E., Peelle, B., Armstrong, R., Demo, S.D., Ferrick, D.A., **Hitoshi,Y.**, Payan, D.G. and Anderson, D. Stable, stoichiometric delivery of diverse protein functions. (**2004**) *Journal of Biochemcal and Biophysical Methods* 58, 101-110.

Patent

1. Toso, a cell-surface specific regulator of Fas-induced apoptosis in T cells
Stanford Docket S98-019